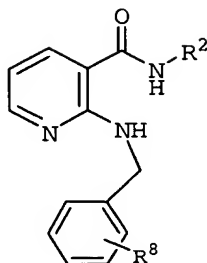


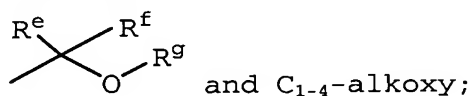
**WHAT IS CLAIMED IS:**

## 1. Compound of Formula IV

**IV**

wherein R<sup>2</sup> is selected from unsubstituted or substituted phenyl, and 9-10 membered bicyclic and 11-14 membered tricyclic unsaturated or partially unsaturated heterocyclyl, wherein substituted R<sup>2</sup> is optionally substituted with one or more substituents selected from halo, C<sub>1-6</sub>-alkyl, optionally substituted C<sub>3-6</sub>-cycloalkyl, optionally substituted phenyl, optionally substituted phenyl-C<sub>1-4</sub>-alkylenyl, C<sub>1-2</sub>-haloalkoxy, optionally substituted phenoxy, optionally substituted 4-6 membered heterocyclyl-C<sub>1-6</sub>-alkyl, optionally substituted 4-6 membered heterocyclyl-C<sub>2-4</sub>-alkenyl, optionally substituted 4-6 membered heterocycliloxy, optionally substituted 4-6 membered heterocyclyl-C<sub>1-4</sub>-alkoxy, optionally substituted 4-6 membered heterocyclylsulfonyl, optionally substituted 4-6 membered heterocyclylamino, optionally substituted 4-6 membered heterocyclylcarbonyl, optionally substituted 4-6 membered heterocyclyl-C<sub>1-4</sub>-alkylcarbonyl, optionally substituted 4-6 membered heterocyclylcarbonyl-C<sub>1-4</sub>-alkyl, optionally substituted 4-6 membered heterocyclyl-C<sub>1-4</sub>-alkylcarbonylamino, optionally substituted 4-6 membered heterocyclyl-

oxycarbonylamino, C<sub>1-2</sub>-haloalkyl, C<sub>1-4</sub>-aminoalkyl,  
 nitro, amino, C<sub>1-3</sub>-alkylsulfonylamino, hydroxy, cyano,  
 aminosulfonyl, C<sub>1-2</sub>-alkylsulfonyl, halosulfonyl, C<sub>1-4</sub>-  
 alkylcarbonyl, amino-C<sub>1-4</sub>-alkylcarbonyl, C<sub>1-3</sub>-  
 5 alkylamino-C<sub>1-4</sub>-alkylcarbonyl, C<sub>1-3</sub>-alkylamino-C<sub>1-4</sub>-  
 alkylcarbonylamino, C<sub>1-4</sub>-alkoxycarbonyl-C<sub>1-4</sub>-alkyl, C<sub>1-3</sub>-  
 alkylamino-C<sub>1-3</sub>-alkyl, C<sub>1-3</sub>-alkylamino-C<sub>1-3</sub>-alkoxy, C<sub>1-3</sub>-  
 alkylamino-C<sub>1-3</sub>-alkoxy-C<sub>1-3</sub>-alkoxy, C<sub>1-4</sub>-alkoxycarbonyl,  
 C<sub>1-4</sub>-alkoxycarbonylamino-C<sub>1-4</sub>-alkyl, C<sub>1-3</sub>-  
 10 alkylsulfonylamino-C<sub>1-3</sub>-alkoxy, C<sub>1-4</sub>-hydroxyalkyl,



wherein R<sup>e</sup> and R<sup>f</sup> are independently selected from H and C<sub>1-2</sub>-  
 haloalkyl;

wherein R<sup>g</sup> is selected from H, C<sub>1-3</sub>-alkyl, optionally  
 15 substituted phenyl-C<sub>1-3</sub>-alkyl, 4-6 membered  
 heterocyclyl, and optionally substituted 4-6 membered  
 heterocyclyl-C<sub>1-3</sub>-alkyl, C<sub>1-3</sub>-alkoxy-C<sub>1-2</sub>-alkyl and C<sub>1-3</sub>-  
 alkoxy-C<sub>1-3</sub>-alkoxy-C<sub>1-3</sub>-alkyl; and

wherein R<sup>8</sup> is one or more substituents independently  
 20 selected from halo, amino, nitro, hydroxy, C<sub>1-6</sub>-alkyl, C<sub>1-6</sub>-  
 haloalkyl, C<sub>1-6</sub>-alkoxy, C<sub>1-6</sub>-haloalkoxy, C<sub>1-6</sub>-aminoalkyl,  
 C<sub>1-6</sub>-hydroxyalkyl, optionally substituted phenyl,  
 optionally substituted heterocyclyl, optionally  
 substituted heterocyclyl-C<sub>1-6</sub>-alkoxy, aminosulfonyl, C<sub>3-6</sub>-  
 25 cycloalkyl, C<sub>1-6</sub>-alkylamino, C<sub>1-6</sub>-alkylamino-C<sub>1-6</sub>-alkyl,  
 optionally substituted heterocyclyl-C<sub>1-6</sub>-alkylamino,  
 optionally substituted heterocyclyl-C<sub>1-6</sub>-alkyl, C<sub>1-6</sub>-  
 alkylamino-C<sub>2-4</sub>-alkynyl, C<sub>1-6</sub>-alkylamino-C<sub>1-6</sub>-alkoxy, C<sub>1-6</sub>-  
 alkylamino-C<sub>1-6</sub>-alkoxy-C<sub>1-6</sub>-alkoxy, and optionally  
 30 substituted heterocyclyl-C<sub>2-4</sub>-alkynyl;

and pharmaceutically acceptable isomers and derivatives  
 thereof;

provided R<sup>2</sup> is not 3-trifluoromethylphenyl when R<sup>8</sup> is 4-hydroxy or 3-hydroxy.

2. Compound of Claim 1 wherein R<sup>2</sup> is selected from  
5 phenyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl,  
1',2'-dihydro-spiro[cyclopropane-1,3'-[3H]indol]-6'-yl,  
isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-  
indolyl, naphthyridinyl, 1,2,3,4-tetrahydro-  
[1,8]naphthyridinyl, dihydrobenzo[1,4]oxaxinyl,  
10 quinoxalinyl, benzo[d]isothiazolyl, 3,4-dihydro-  
quinazolinyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl,  
5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl,  
tetrahydroquinolinyl, indazolyl, 2,1,3-benzothiadiazolyl,  
benzodioxanyl, benzothienyl, benzofuryl, benzimidazolyl,  
15 dihydro-benzimidazolyl, benzoxazolyl and benzthiazolyl,  
where R<sup>2</sup> is unsubstituted or substituted with one or more  
substituents selected from bromo, chloro, fluoro, iodo,  
nitro, amino, cyano, Boc-aminoethyl, hydroxy, oxo,  
fluorosulfonyl, methylsulfonyl, aminosulfonyl, 4-  
20 methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl,  
4-pyridylmethyl, 4-morpholinylmethyl, 1-methylpiperazin-4-  
ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl,  
piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-  
methyl-2-(1-methylpiperidin-4-yl)ethyl, 2-methyl-2-(4-  
25 pyrimidinyl)ethyl, 2-methyl-2-(5-methyloxadiazol-2-yl)ethyl,  
2-methyl-2-(pyrazol-5-yl)ethyl, 2-methyl-2-(1-  
ethoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)ethyl,  
morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, 1-  
(4-morpholinyl)-2,2-dimethylethyl, piperidin-4-ylethyl, 1-  
30 Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-  
piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-  
4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-  
ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl,  
pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, 1-

(pyrrolidin-1-yl)-2-methylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, 2-methyl-2-(pyrrolidin-1-yl)ethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, pyrrolidin-1-yl-carbonyl, pyrrolidin-2-yl-carbonyl, 4-pyridylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl,  $\text{CH}_3\text{O}-\text{C}(=\text{O})-\text{CH}_2-$ , methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, methylsulfonylamino, dimethylaminomethylcarbonylamino, 1-pyrrolidinyl- $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-$ , 4-morpholinyl- $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-$ , 3-tetrahydrofuryl- $\text{O}-\text{C}(=\text{O})-\text{NH}-$ , cyclohexyl- $\text{N}(\text{CH}_3)-$ , (4-pyrimidinyl)amino, (2-methylthio-4-pyrimidinyl)amino, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(pyrrolidin-2-ylmethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, 3-tetrahydrofuryloxy, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, 3-tetrahydrofurylmethoxy, pyrrolidin-2-ylmethoxy, 1-methylcarbonyl-pyrrolidin-2-ylmethoxy, 1-Boc-pyrrolidin-2-ylmethoxy, pyrrolidin-1-ylmethoxy, 1-methyl-pyrrolidin-2-ylmethoxy, 1-isopropyl-pyrrolidin-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, (1-pyrrolidinyl)ethoxy, piperdin-4-ylmethoxy, piperdin-3-ylmethoxy, 1-methylpiperdin-4-yloxy,

methylsulfonylaminoethoxy, isopropoxy, methoxy and ethoxy; and pharmaceutically acceptable isomers and derivatives thereof.

5           3. Compound of Claim 1 wherein R<sup>8</sup> is one or more substituents independently selected from chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, -O-CH<sub>2</sub>-O-, trifluoromethoxy, 1-methylpiperidinylmethoxy, dimethylaminoethoxy, amino, dimethylamino,  
10 dimethylaminopropyl, diethylamino, aminosulfonyl, cyclohexyl, dimethylaminopropynyl, 3-(4-morpholinyl)propyn-1-yl, dimethylaminoethoxyethoxy, 3-(4-morpholinyl)propylamino, optionally substituted piperidinyl, morpholinyl, optionally substituted piperazinyl, optionally  
15 substituted phenyl, methyl, ethyl, propyl, cyano, hydroxymethyl, aminomethyl and trifluoromethyl; and pharmaceutically acceptable derivatives thereof.

          4. Compound of Claim 2 wherein R<sup>2</sup> is selected from  
20 1,2,3,4-tetrahydro-isoquinolyl optionally substituted with one or more substituents selected from methyl, and Boc,  
1,2,3,4-tetrahydro-quinolyl optionally substituted with one or more substituents selected from methyl, Boc and  
25 oxo,  
2,3-dihydro-1H-indolyl optionally substituted with one or more substituents selected from methyl, methylsulfonyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-yl, piperidin-4-yl, 1-  
30 methyl-piperidin-4-ylmethyl, 1-methyl-piperidin-4-yl, pyrrolidin-1-yl-carbonyl, dimethylaminomethylcarbonyl, aminomethylcarbonyl, methylcarbonyl, pyrrolidin-2-ylmethyl, and 1-Boc-pyrrolidin-2-ylmethyl, and

3,4-dihydro-2H-benzo[1,4]oxazinyl optionally substituted with one or more substituents selected from methyl, and methylcarbonyl; and pharmaceutically acceptable derivatives thereof.

5

5. Compound of Claim 4 wherein R<sup>2</sup> is 3,3-dimethyl-2,3-dihydro-1H-indolyl optionally substituted with a substituent selected from pyrrolidin-1-yl-carbonyl, methylcarbonyl, and methylsulfonyl; and pharmaceutically acceptable derivatives thereof.

10

6. Compound of Claim 4 wherein R<sup>2</sup> is 4,4-dimethyl-1,2,3,4-tetrahydro-1H-isoquinoliny1.

15

7. Compound of Claim 3 wherein R<sup>8</sup> is one or more substituents independently selected from fluoro, hydroxy, amino, and nitro; and pharmaceutically acceptable derivatives thereof.

20

8. Compound of Claim 3 wherein R<sup>8</sup> is 4-fluoro; and pharmaceutically acceptable derivatives thereof.

9. Compound of Claim 1 wherein R<sup>2</sup> is selected from phenyl substituted with one or more substituents selected from chloro, tert-butyl, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, dimethylaminomethylcarbonylamino, 1,1-di(trifluoromethyl)-1-(pyrrolidin-2-ylmethoxy)methyl, trifluoromethyl, 2-methyl-2-(morpholin-4-yl)ethyl, 2-methyl-2-(pyrrolidin-1-yl)ethyl, 2-methyl-2-(5-methyloxadiazol-2-yl)ethyl, methylsulfonylamino, 1-methyl-pyrrolidin-2-ylmethoxy, and isopropyl; and pharmaceutically acceptable derivatives thereof.

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10. A compound and pharmaceutically acceptable salts thereof selected from:

- 5 N-(3,3-Dimethyl-1-(methylsulfonyl)-2,3-dihydro-1H-indol-6-yl)-2-(((4-fluorophenyl)methyl)amino)-3-pyridinecarboxamide;  
N-(4-(1,1-dimethylethyl)-3-((N,N-dimethylglycyl)amino)phenyl)-2-(((4-fluorophenyl)methyl)amino)-3-pyridinecarboxamide;  
10 N-(3-(((2R)-1-methyl-2-pyrrolidinyl)methyl)oxy)-5-(trifluoromethyl)phenyl)-2-((3-(1,3-oxazol-5-yl)phenyl)amino)-3-pyridinecarboxamide;  
2-(((4-fluorophenyl)methyl)amino)-N-(3-(((2R)-1-methyl-2-pyrrolidinyl)methyl)oxy)-5-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;  
15 2-(((4-fluorophenyl)methyl)amino)-N-(3-((methylsulfonyl)amino)-5-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;  
20 2-((3-(1,3-oxazol-5-yl)phenyl)amino)-N-(3-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;  
2-(((4-fluorophenyl)methyl)amino)-N-(4-(1-methyl-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethyl)phenyl)-3-pyridinecarboxamide;  
25 3-(2-Chloro-5-{{2-(4-fluoro-benzylamino)-pyridine-3-carbonyl]-amino}-phenoxy)methyl)-azetidine-1-carboxylic acid tert-butyl ester;  
N-[3-(Azetidin-3-ylmethoxy)-4-chloro-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;  
30 6-Chloro-3-(4-fluoro-benzylamino)-pyridazine-4-carboxylic acid (4-tert-butyl-phenyl)-amide;  
3-(4-Fluoro-benzylamino)-pyridazine-4-carboxylic acid (4-tert-butyl-phenyl)-amide;

2-(4-Hydroxy-3-amino-benzylamino)-N-(4-isopropyl-phenyl)-  
nicotinamide ;

2-(4-Hydroxy-3-nitro-benzylamino)-N-(4-isopropyl-phenyl)-  
nicotinamide;

5 3-(4-Fluoro-benzylamino)-1,2,5,6-tetrahydro-pyridazine-4-  
carboxylic acid (4-*tert*-butyl-phenyl)-amide; and  
N-[3-(Azetidin-3-ylmethoxy)-5-trifluoromethyl-phenyl]-2-(4-  
fluoro-benzylamino)-nicotinamide.

10 11. A pharmaceutical composition comprising a  
pharmaceutically-acceptable carrier and a compound as in any  
of Claims 1-10.

15 12. A method of treating cancer in a subject, said  
method comprising administering an effective amount of a  
compound as in any of Claims 1-10.

20 13. The method of Claim 12 comprising a combination  
with a compound selected from antibiotic-type agents,  
alkylating agents, antimetabolite agents, hormonal agents,  
immunological agents, interferon-type agents and  
miscellaneous agents.

25 14. A method of treating angiogenesis in a subject,  
said method comprising administering an effective amount of  
a compound as in any of Claims 1-10.

30 15. A compound as in any of Claims 1-10 for use in a  
method of therapeutic treatment for the human or animal  
body.

35 16. A method of treating KDR-related disorders in a  
mammal, said method comprising administering an effective  
amount of a compound as in any of Claims 1-10.

17. A method of treating proliferation-related  
disorders in a mammal, said method comprising administering  
an effective amount of a compound as in any of Claims 1-10.



18. A method of reducing blood flow in a tumor in a subject, said method comprising administering an effective amount of a compound as in any of Claims 1-10.

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19. A method of reducing tumor size in a subject, said method comprising administering an effective amount of a compound as in any of Claims 1-10.

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20. A method of treating diabetic retinopathy in a subject, said method comprising administering an effective amount of a compound as in any of Claims 1-10.

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